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RELATION BETWEEN PLASMA K^+ AND VENTILATION DURING INCREMENTAL EXERCISE AFTER GLYCOGEN DEPLETION AND REPLETION IN MAN

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SUMMARY

1. We have examined the relationship between expiratory ventilation ($\dot{V}_E$), plasma potassium concentration ($[K^+]_P$), blood lactate concentration ($[Lac^-]_B$), and plasma pH (pH_P) in five trained men before and after glycogen depletion and repletion in two successive incremental bicycle ergometer tests (tests A and B).

2. Though pH_P was significantly higher after glycogen depletion (in relation to normal or repleted conditions) $\dot{V}_E$ and $[K^+]_P$ also tended to be higher.

3. There was no constant relation between the magnitude or the direction of change in lactic acidosis, or $\dot{V}_E$ and $[K^+]_P$, respectively. Instead, a close temporal relationship between changes in $\dot{V}_E$ and $[K^+]_P$ was found.

4. A non-linear increase in $\dot{V}_E$ occurred independently of changes in pH_P or $[Lac^-]_B$, but could be well predicted from a non-linear increase in $[K^+]_P$.

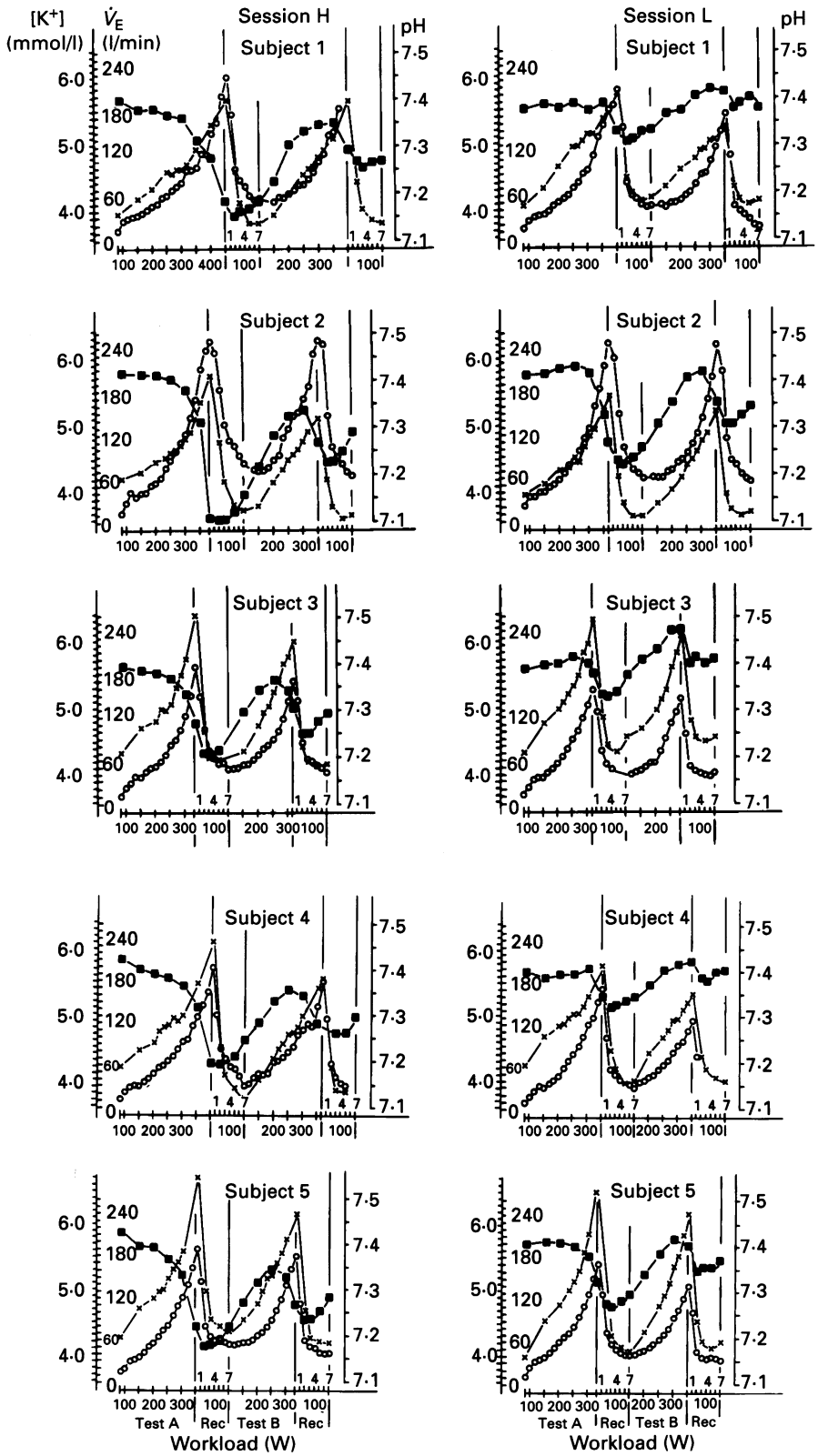
5. These findings indicate that lactic acidosis had no deciding effect on exercise ventilation in these experiments. They are consistent with the idea that the potassium increase may contribute to the ventilatory drive during exercise.

INTRODUCTION

Stimulation of arterial chemoreceptors by lactic acidosis is often thought to be responsible for ventilatory drive characteristics during heavy exercise (e.g. Wasserman, Whipp, Koyal & Cleary, 1975). On the other hand a number of studies indicate that acidosis and ventilation may not be cause and effect (e.g. Hagberg, Coyle, Carroll, Miller, Martin & Brooke, 1982; Heigenhauser, Sutton & Jones, 1983; Busse & Maassen, 1987; Conway, Paterson, Petersen & Robbins, 1988; Paterson, Friedland, Bascom, Clement, Cunningham, Painter & Robbins, 1990).

Recent research suggests that potassium may act as a potent stimulus of ventilation during exercise (e.g. Tibes, 1981; Band, Linton, Kent & Kurer, 1985; Busse & Maassen, 1987; Paterson & Nye, 1988; Busse, Maassen, Konrad & Böning, 1989; Paterson *et al.* 1990).

This paper examines the relationship between plasma potassium, ventilation and acid–base status during two successive incremental exercise tests in normal


[K+] (mmol/l)
V̇E (l/min)
Session H
Session L
Subject 1
Subject 2
Subject 3
Subject 4
Subject 5
pH
Test A
Rec
Test B
Rec
Workload (W)

conditions and after glycogen depletion and repletion, i.e. during more or less acidotic conditions and during increasing or decreasing lactic acidosis.

METHODS

Five male endurance-trained healthy subjects (22–31 years, mean 27 ± 3 years, $\dot{V}_{O_2,max}$ (maximum oxygen uptake) 4·7 ± 0·6 l) participated in the study after giving written informed consent. The first test session ('normal' glycogen stores, 'N') was performed after 2 days without training and with the subjects normal diet. After this test the subjects had a low-carbohydrate diet combined with training to decrease the muscle glycogen stores, followed by the second test session (low glycogen stores, 'L'). After an additional 3 days with a carbohydrate-rich diet without training, the third session was performed (repleted, high glycogen stores, 'H'). Each test session consisted of two succeeding incremental bicycle ergometer tests (tests A and B), each followed by a 7 min recovery (recoveries A and B). The workload was increased by 16·7 W/min (corresponding to 50 W/3 min) until exhaustion. The blood was arterialized using a warm-water floated glove (about 43 °C on the skin). Blood samples (5 ml) were drawn into heparinized syringes through an 18 G Teflon catheter, inserted into the forearm vein, immediately before the tests, every 50 W during test A and B and immediately before exhaustion, and at the end of the second, third, fifth and seventh minute of the recovery periods. A 2 ml aliquot was centrifuged immediately for the determination of plasma potassium concentration ($[K^+]_P$) by an ion-selective electrode (KNA 1, Radiometer, Copenhagen, Denmark). The remaining blood was stored anaerobically in ice-cold water and plasma pH (pH_P), blood lactate concentration ($[Lac^-]_B$, measurement kit from Boehringer) and plasma proteins (measurement kit from Merck) were measured immediately after the tests. Heart rate (ECG recording) and ventilation parameters ($\dot{V}_E$, $\dot{V}_{O_2}$) were recorded each minute. $\dot{V}_E$ and $\dot{V}_{O_2}$ were measured in a closed system (Magnatest Meditron, Buckholz, Germany).

Statistical evaluation

The values are given as single values or as means ± standard deviation (S.D.). Differences between the tests were calculated by a repeated measures analysis of variance and the Scheffe' test or the *t* test for repeated measurements. $P < 0·05$ was set as significant. The values at the end of test A and B are referred to as 'maximum' values.

RESULTS

Figure 1 shows the responses of pH_P, $\dot{V}_E$ and $[K^+]_P$ to the succeeding incremental exercise tests (A and B) and the recovery periods of the five subjects. The respective means are displayed in Fig. 2.

Comparison between the three test sessions

From 200 W on, $[Lac^-]_B$ was significantly higher in session N and H than in L. pH_P values were significantly lower from 250 W on (the differences can be read approximately from Fig. 2). $\dot{V}_E$ for test A was significantly higher in session L than

Fig. 1. Single values. Changes in $[K^+]_P$ (×), $\dot{V}_E$ (○) and pH_P (■) during two succeeding incremental exercise test (tests A and B) after glycogen depletion (L) and glycogen repletion (H). Note that $[K^+]_P$, $\dot{V}_E$ and pH_P followed a similar time course only in test A. During the first minutes of recovery (Rec), pH continued to decrease in session H, when $\dot{V}_E$ and K^+ were also decreasing. The changes of $\dot{V}_E$ and $[K^+]$ were very similar in all tests, though in the B tests pH was progressively increasing and was reaching even slightly alkaline values in L.

in N from 217 W on, and also higher in session L than in H from 250 W on. In the recovery periods or test B there were no significant differences. $[K^+]_P$ tended to be higher in tests A and B for session L, compared to N and R, though these differences were not significant (Fig. 2).

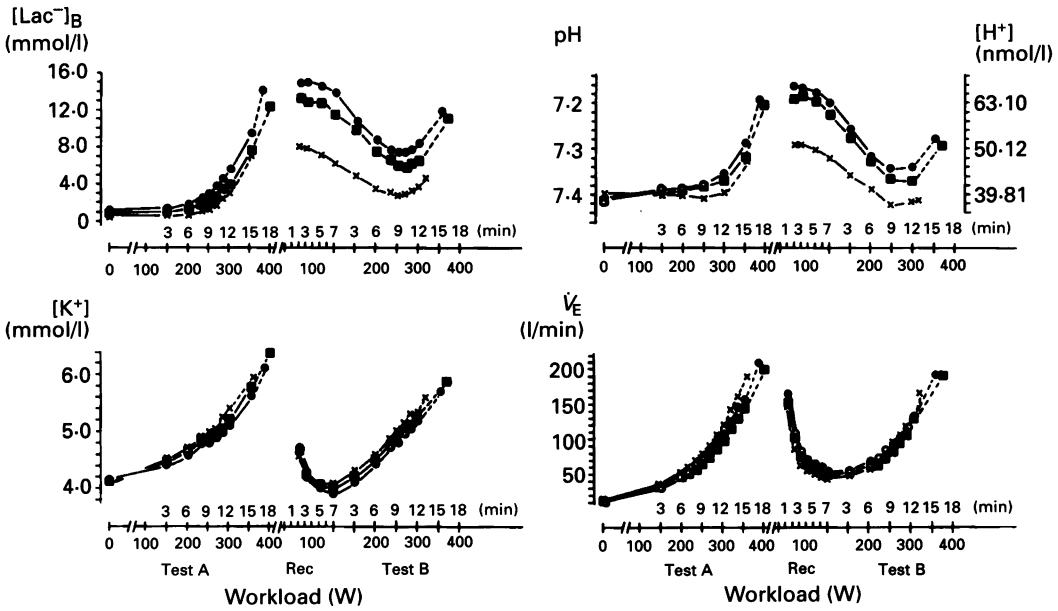


Fig. 2. Means. Changes in $[K^+]_P$, pH_P and $\dot{V}_E$, $[Lac^-]_B$ during two succeeding incremental exercise tests (tests A and B) during normal conditions (N, ■), after glycogen depletion (L, ×) and glycogen repletion (H, ●). Note the tendency to higher $[K^+]_P$ in session L, tests A and B, and higher $\dot{V}_E$ in session L, test A.

Examination of the direction of change of the variables in tests A and B and the recovery periods

On all three occasions (N, L and R) pH_P was decreasing and $[Lac^-]_B$ was increasing in test A, while there was a marked increase of pH_P and decrease of $[Lac^-]_B$ in test B until about 250 W. In session L even the maximum values of test B tended to be alkalotic. The $\dot{V}_E$ and $[K^+]_P$ increases were similar throughout tests A and B (Figs 1 and 2). In the recovery period, even in the fifth minute, pH_P and $[Lac^-]_B$ were markedly lower and higher, respectively, than the maximum values, while $\dot{V}_E$ and $[K^+]_P$ decreased considerably during the same time period (Figs 1 and 2).

Relationship between the non-linear increase in $\dot{V}_E$ ('ventilatory threshold') and metabolic responses

The non-linear increase in ventilation could not be related to any of the usual 'anaerobic or aerobic thresholds' as determined from an increase of $[Lac^-]_B$ of 1 or 2 mmol/l of blood above resting levels, from a $[Lac^-]_B$ of 4 mmol/l of blood, or from a decrease of pH_P below 7·35 (Table 1). The best prediction of the non-linear increase in $\dot{V}_E$ was obtained from a non-linear increase in $[K^+]_P$ (Table 1).

DISCUSSION

Arterialization of venous blood

According to Forster, Dempsey, Vidruk & Do Pico (1972) arterialization with a temperature of about 43 °C on the skin provides valid estimation of arterial P_{CO_2} and pH. A K^+ uptake may occur in resting muscles and thus K^+ measurements using the

TABLE 1. Differences in workload of various aerobic or anaerobic thresholds

	Thresholds					
Session/test	t_1	t_2	t_4	t_{ILEP}	t_{K^+}	$t_{7\cdot35}$
N/A	−24±35	9±24	34±20	−11±38	3±22	54±43
N/B	−28±43	5±34	30±32	−15±38	14±22	
L/A	10±19	41±19	65±20	−6±12	10±15	83±37
L/B	13±47	44±35	68±35	−3±29	−14±22	
H/A	−47±30	−13±25	8±30	−12±22	0±21	37±30
H/B	−47±29	−13±29	8±37	−12±24	0±12	
all	−20±39	12±35	36±36	−10±27	2±20	

Thresholds compared with a non-linear increase in ventilation: lactate thresholds at 1 and 2 mmol/l above resting levels (t_1 and t_2), at 4 mmol/l (t_4), at the individual lactate equilibration point as determined in test B (t_{ILEP}, corresponding to the minimum of the workload lactate curve), at pH 7·35 ($t_{7\cdot35}$, corresponding to beginning acidosis). In addition, a point of non-linear increase of $[K^+]_P$ (t_{K^+}) was used. The means of the differences are given ±standard deviation (threshold workloads below the ventilatory threshold are given as negative values. N/A, e.g. corresponds to session N, test A).

blood of deep arm veins may underestimate arterial values (Coats, 1986). It has been calculated that this difference is distinctly less than 5% if arterialized blood of superficial forearm veins is used (Busse & Maassen, 1989).

Glycogen depletion and repletion

Though glycogen stores were not directly measured, the intended effect, a marked reduction of exercise acidosis for given workloads, was attained. A certain overcompensation apparently occurred due to the glycogen repletion regimen (note higher lactate levels and more acidotic pH_P in session H, Figs 1 and 2).

Ventilation

Our results correspond with other data on exercise ventilation before and after glycogen depletion (Heigenhauser *et al.* 1983; Busse & Maassen, 1987) where no difference in ventilation, in spite of markedly differing pH_P values, was found. The theoretical approach in these experiments is near to that of studies in McArdle's patients, with comparable results (Hagberg *et al.* 1982; Hagberg, King, Rogers, Montain, Jilka, Kohrt & Heller, 1989; Paterson *et al.* 1990): whereas the production of lactic acid in glycogen depleted subjects may be markedly reduced, McArdle's subjects will produce no acid at all. The higher $\dot{V}_E$ in the glycogen-depleted state may be due to the higher subjective effort for a given load, including activation of auxiliary muscles. The slightly higher potassium increase after glycogen depletion could also have the same explanation. The present experiments suggest that exercise

acidosis and ventilation are hardly cause and effect: while the increase in non-volatile acid and the non-linear increase in ventilation in an incremental exercise test during normal conditions (e.g. session N, test A) would reveal an apparently good correlation, the tests after glycogen depletion and mainly the 'B' tests of this series, demonstrate that this close temporal relationship would be merely coincidental.

Plasma potassium

$[K^+]_P$ response to incremental exercise was very similar in all tests (Fig. 2), though a tendency to higher values was noted in session L, perhaps due to the generation of a greater number of action potentials for a given workload in this test. This may be a result of depleted energy stores in the exercising muscles and an additional activation of auxiliary muscles. Several explanations for the potassium increase during exercise have been discussed. A model which would provide a satisfying explanation for both, the exponential potassium increase during exercise and for the rapid re-uptake of potassium in the first minutes of recovery, is based on the fact that the activity of renal microsomal Na^+,K^+-ATPase is markedly inhibited by an increase in intracellular inorganic phosphate $[P_i]$ (Huang & Askari, 1984). Relating these data to intracellular $[P_i]$, temperature and pH changes as occur during exercise (Taylor, Styles, Matthews, Arnoled, Gadian, Bore & Radda, 1986), the exponential increase in $[K^+]_P$ could well be related to an increasing inhibition of Na^+,K^+-ATPase by an increase in intracellular $[P_i]$, while an ATPase-inhibiting pH decrease and a temperature-stimulating increase would cancel each other (Park, 1983). During the first minutes of recovery a marked decrease in intracellular $[P_i]$ due to resynthesis of phosphocreatine, the increasing intracellular pH (Taylor *et al.* 1986) and the increased temperature would then explain the rapid decrease of plasma $[K^+]_P$ even to subnormal values. Other known effects on $[K^+]_P$ changes during and after exercise such as catecholamine changes (e.g. Carlsson, Fellenius, Lundborg & Svensson, 1978) would not be affected by this hypothesis.

The control of exercise hyperpnoea

The idea that acid may act as an important ventilatory stimulus, not only in rest but also during exercise, is based on the often observed close temporal relationship between the increase of lactic acid and ventilation in incremental exercise. Particularly, results of Wasserman *et al.* (1975), who found that ventilatory transients were markedly slowed in patients without carotid bodies, supported the opinion that the respiratory compensation for exercise-induced metabolic acidosis may be mediated by the carotid bodies. The determination of the so called anaerobic threshold using a non-linear increase in $\dot{V}_E$ is also based on this idea. In accord with studies in McArdle's patients (e.g. Paterson *et al.* 1990), the present experiments indicate that the correlation between a marked increase in plasma $[H^+]$ and the overproportional increase in ventilation is merely coincidental and not cause and effect. On the other hand a good correlation between the non-linear increase in $\dot{V}_E$ and a non-linear increase in $[K^+]_P$ has been found in these (Table 1) and other experiments (Bascom, Clement, Cunningham, Friedland, Paterson & Robbins, 1989; Paterson *et al.* 1990), independently of the acid–base status. The results of Wasserman *et al.* (1975) may be well explained by the observation that the carotid

bodies are sensitive to increased $[K^+]_P$ (Linton & Band, 1985; Paterson & Nye, 1988). The K^+-induced increase in $\dot{V}_E$ can be abolished by peripheral chemoreceptor denervation (Band *et al.* 1985). Relating these facts to the data of Wasserman *et al.* (1975), who found that carotid body resection caused slowed ventilatory transients but no decrease in the magnitude of the ventilatory response to a given workload, it appears that the effect of $[K^+]_P$ via the arterial chemoreceptors is a more qualitative than quantitative one. An additional cardiorespiratory drive may be related to the effects of increased interstitial K^+ accumulation via C3/4 afferents (McCloskey & Mitchell 1972; Tibes, 1981). In conclusion, (1) it is improbable that acid was a relevant stimulus of $\dot{V}_E$ during incremental exercise in these experiments; (2) the 'anaerobic threshold' concept should be revised; the non-linear increase in $\dot{V}_E$ in relation to workload is not an effect of increasing lactic acidosis; (3) the close relationship between $[K^+]_P$ and $\dot{V}_E$ during exercise in subjects with normal, depleted and repleted glycogen stores supports the role of this ion as a potent stimulus of exercise ventilation.

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